June 16, 2003

Elmer Rauckman, Ph.D., DABT
Consulting Toxicologist
BPPB Consortium
1201 Anise Court
Freeburg, IL 62243

Dear Dr. Rauckman:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2-Pyrrolidone posted on the ChemRTK HPV Challenge Program Web site on January 31, 2003. I commend The BPPB Consortium on behalf of the 2-Pyrrolidone Consortium for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The BPPB Consortium on behalf of the 2-Pyrrolidone Consortium advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
2-Pyrrolidone

Summary of EPA Comments

The sponsor, the 2-Pyrrolidone Consortium, submitted a test plan and robust summaries to EPA for 2-pyrrolidone (CAS No. 616-45-5) dated December 30, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 31, 2003.

EPA has reviewed this submission and reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. Adequate data are available for all endpoints for the purposes of the HPV Challenge Program.

2. Health Effects. Adequate data are available for all endpoints except reproductive toxicity for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of the reproductive toxicity data pending receipt of more details of the histopathology on reproductive organs from the submitted 90-day rat study. The submitter needs to address deficiencies in some robust summaries.

3. Ecological Effects. Adequate data are available for all endpoints for the purposes of the HPV Challenge Program

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the 2-Pyrrolidone Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

Adequate data are available for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Adequate data are available for the purposes of the HPV Challenge Program.

Biodegradation. EPA agrees that available data for this endpoint are adequate. While it is inappropriate to use an inherent biodegradation study to draw conclusions about ready biodegradation, and BIOWIN estimates are insufficient to adequately address this endpoint, the submitted data including the ready biodegradation study for the analogue N-methyl-2-pyrrolidone satisfy the endpoint for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for the purposes of the HPV Challenge Program except for reproductive toxicity.

Reproductive Toxicity. EPA reserves judgement on the adequacy of available reproductive toxicity data pending receipt of more details of the histopathology on male and female reproductive organs from the

submitted 90-day oral study in rats. These data, if adequate, plus data from the oral developmental toxicity study in rats will satisfy the reproductive toxicity endpoint for the purposes of the HPV Challenge Program. The submitter needs to include all relevant data in a separate robust summary for this endpoint.

Ecological Effects (fish, invertebrates, and algae)

Adequate data are available for all ecotoxicity endpoints for the purposes of the HPV Challenge Program. However, for the acute fish toxicity study, the submitter needs to express the LC_{50} as the geometric mean of the two highest concentrations in order to be consistent with OECD Guideline 203.

The submitter also needs to address more fully and, if possible, explain the disagreement between the EC_{50} values reported for Daphnia magna (48-h EC_{50} >500 mg/L and 96-h EC_{50} >10,000 mg/L) and Daphnia pulex (48-h EC_{50} = 13.21 mg/L).

Specific Comments on the Robust Summaries

Environmental Fate

Biodegradation. The robust summary of the 2-pyrrolidone study is unclear as to whether this is an inherent or a ready biodegradation study. The methodology is stated as following the Zahn-Wellens test procedure, which is used for testing inherent biodegradation. However, the summary states that it uses "non-adapted sludge flora," which indicates a ready biodegradation study. The summary also states that "...the conditions do not meet the OECD 301 series." The OECD 301 series is for ready biodegradation and the OECD 302 series is for inherent biodegradation. The test temperature was not reported.

Health Effects

Acute Toxicity. The submitter needs to provide the following information: the length of the observation period, necropsy analyses (if performed), and a range or 95% confidence interval for the LD_{50}.

Repeated-Dose Toxicity. The submitter needs to include the magnitude of the kidney weight changes and identify the organs that were examined for gross pathology and histopathology, especially those associated with reproduction.

Ecological Effects

Fish and Invertebrates. The submitter needs to indicate whether the toxicity values from critical studies were based on measured or nominal concentrations and provide missing information on GLP compliance in the summary of the acute invertebrate study.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.